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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/183,375	10/30/1998	JANOS SZEBENI	003/098/SAP	3056

7590 07/06/2005

THOMAS G. WISEMAN
VENABLE, BAETJER, HOWARD & CIVILETTI LLP
SUITE 1000
1201 NEW YORK AVENUE, N. W.
WASHINGTON, DC 20005

EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 07/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/183,375	SZEBENI ET AL.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,10,16,17 and 20-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6, 10, 16-17 and 20-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment dated 4-15-05 is acknowledged.

Claims included in the prosecution are 1-4, 6, 10, 16-17 and 20-22.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 is confusing. What is being conveyed by "In a method for treating a patient involving a pharmaceutical composition ---"?

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-4, 6, 10, 16-17 and 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Terwogt (cancer Treatment Reviews, March 1997) or O'Brien (Annals of Oncology, 1992) in view of Ko (5,851,528).

Terwogt teaches that that the antitumor drug paclitaxel is usually administered in combination with the vehicle, cremophor EL (polyethoxylated castor oil) and the administration of this combination causes severe hypersensitivity reactions (pages 88-89). What is lacking in Terwogt is the teaching of the administration of compliment activation inhibitors.

O'Brien teaches that several cytotoxic drugs including Taxol and doxorubicin cause hypersensitivity reactions (abstract and Table 2).

Ko teaches that compliment system includes a group of proteins in blood plasma, which plays an integral role in immune and allergic reaction and discloses a method of inhibiting complement activation by administering complement activation inhibitors. The method involves the administration of the inhibitor in controlled release delivery devices such as liposomes. The method is used for various conditions including the drug induced allergies and inflammation (note the abstract, col. 3, lines 49-52, col. 5, lines 32-51, col. 11, lines 1-42, examples and claims). Ko is also suggestive of the administration of the inhibitor along with the drug from his statements on col. 10, line 42 et seq., according to which the inhibitor "can be combined with appropriate pharmaceutical formulation. Ko however, does not specifically teach instant drugs or carriers such as Cremophors.

In essence the reference of Terwogt shows the problems (hypersensitivity) associated with the commonly used drug-carrier (paclitaxel-Cremophor) combination and that of O'Brien shows that several drugs cause allergic (hypersensitivity) reactions.The reference of Ko offers a solution.

To use compliment activation inhibitors to reduce or inhibit the hypersensitivity reactions caused by paclitaxel-cremophor EL combination or that caused by drugs such as doxorubicin and others would have been obvious to one of ordinary skill in the art since Ko teaches that such an administration would reduce the allergies and inflammation caused by the drugs. The criticality of the administration of the compliment activation inhibitor prior to the administration of the drug is unclear to the examiner since it would be obvious to one of ordinary skill in the art that such an administration would prevent the active agent or the carrier from activation of the compliment system. The criticality of the active agent in claim 17 is also unclear to the examiner since the claims are drawn to the inhibition of the hypersensitivity reactions by the compliment activation inhibitor and hemoglobin is known to be administered to anemic patients. Compliment inhibition by the inhibitor occurs irrespective of the nature of the drug.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that none of the references unequivocally indicate polyethoxylated oil or derivatized polyethoxylated oil carrier as the causative agent for an immediate hypersensitivity reaction. Applicant further argues that O'Brien reviews allergic reactions to cytotoxic drugs and although both Taxol and Cremophor are mentioned, the nature of the underlying mechanism is not stated by O'Brien. These

arguments are not persuasive since instant claims are not just drawn to these carriers (Cremophor), but in combination with drugs such as taxol and Terwogt teaches the combination of taxol with polyethoxylated castor oil causes hypersensitivity reactions. Furthermore, Terwogt recognizes the effects of polyethoxylated castor oil by itself as evident from page 89 line 1 et seq. Applicant's arguments that none of the references suggest the involvement of the compliment system. This argument is not found to be persuasive since Ko discusses what the compliment system is, its activation and a solution to the compliment activation. Ko's solution is to include the inhibitor along with the agent, which causes the activation leading to hypersensitivey reactions in the host. The examiner disagrees with applicant that Ko adds little to the relevant knowledge of Terwogt since as pointed out above, Ko is suggestive of a solution when there is compliment activation and this suggestion would be the same irrespective of which agent is causing the compliment activation. Applicant's arguments with regard to WO 97/268 are not persuasive since this reference is not used in the rejection. The rejection is maintained.

3. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK

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